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Dear Francis:

I have now returned from my extended trip abroad and am answering your letter of December 5. While I was visiting in India, I saw Sydney Brenner several times and we had a number of detailed discussions about this matter.

You are quite incorrect in your statement that I described the old structure in public while in private selected people were told about the new structure. It is true that I did not use the words "old" and "new" in my lecture. As the transcript shows, the presentation was chronological in outline in that I described earlier crystallographic problems and the interpretations at lower resolution first and then finally discussed the difficulty of "getting the right nucleotide associated with the right peak" in the map. I then went on to say "In our first attempt at this we could follow the chain in a general way and it followed more or less what we had seen at 4Å resolution." Then I went on to say that we "studied these loop regions in more detail." At a later stage I spoke about "our initial tracing" and the fact that we had seen "some features which were correct and some features that we think are incorrect after studying it further." It is quite clear in the context of the talk that I was referring to the results of the earlier March Nature paper. In the Nature paper we described the general tracing as similar to that seen in the 4Å map, but clearly stated that our interpretation was tentative and incomplete in the loop regions.

I then proceeded to make a number of comments about interpretations which were not present at all in the March paper, but were a reinterpretation of the 3Å map. The transcript shows that I made the following specific points in my lecture:

1) I referred both at the beginning of my talk and at the end to the involvement of the constant tRNA bases in tertiary structure interactions. At the very end of my presentation I describe the molecule as one "in which several of the tertiary structure interactions involve the bases that are constant in all transfer RNA's and this suggests that this may indeed be a general type of structure, but we won't know until the structure of other types of tRNA's are worked out." The earlier Nature structure does not use the constant bases in tertiary interactions.

2) Considerable emphasis in my lecture was placed on the chemical reactivity. This included not only a slide discussing the chemical modification reactions in detail (similar to that which was in Figure 1 of our later Science paper), but I also made an explicit statement that there are "a number of tertiary interactions with a folding of the chain which accounts for this." The chemical modification data are not explained by the structure in the earlier Nature paper.

3) As if to emphasize the point that we had reinterpreted the map, I made an explicit statement immediately after Jon Robertus' paper. In his discussion, he said that our D stem was different than his. I stated explicitly that "the bases in the D stem are more or less stacked as you have them and not at right angles," as the latter was his description of how they were stacked in the Nature article. Clearly what I was describing was not in the "old" structure, but rather represented a "new" interpretation. The effect of changing the assignment of nucleotides to the electron density peaks in the D stem clearly changes the assignment of all the residues in the D loop. The net effect of this, of course, is to change the relationship between all of the residues in the D loop with all of the residues in the T ψ C loop.

4) I explicitly mentioned four tertiary interactions in the presentation involving U8-A14, G15-C48, G19-C56 and T54-A58. I also stated that these are "some" of the tertiary interactions that we see. These tertiary interactions were not present in the earlier Nature paper.

5) Finally, near the end I make an explicit statement saying that we have a modified tracing for the anticodon end which is "different from that we saw initially."

The net effect of all of these statements indicated rather clearly that we had changed our interpretation. It may be that Brian Clark did not understand these remarks or did not catch them, but that is not my fault. Our changes in interpretation were apparent to people who were following the structure in detail, and several have so indicated to me. We did not tell other people in private that we had a "new" structure. It is true that during the meeting many

people asked us for more details about these interactions, and that is how they have in their notes additional information about the nature of the hydrogen bonding and the fact that a full paper would be coming out soon with more interactions.

It may be that your colleagues did not recognize that we had changed our interpretation, but their actions suggest that they did. Eight days after the meeting ended they submitted a paper which was rushed into print describing the chemical modification material which they had not included in the first draft of their Nature paper. If they felt there was little new in our interpretation of the map, why would they have rushed so quickly into print?

It is also clear that our interpretation of the map was not uniformly firm throughout the structure. This is seen in the relationship G15-C48. As you will observe in the wording of our Science paper, we were aware of the fact that there could be a reversed WC pairing, but we were not definite. This is because we were also aware of the fact that adopting a syn conformation of the G residue (which is known to adopt syn conformations readily) and an altered pucker of the ribose ring made it possible to make the pair as WC rather than reversed WC. However, these uncertainties in the interpretation of the conformation of one residue did not represent uncertainty elsewhere in the molecule. Indeed, it is clear from their paper that your colleagues also had some regions of uncertain interpretation.

As I readily admitted to you in my letter of August 9, my mistake was in not making a full presentation at the Steenbock meeting and, of course, I continue to bear responsibility for that. However, if there is a full public disclosure I would make absolutely clear the context of my presentation. When we came to the meeting, your colleagues told us that although they had sent in a paper describing their interpretation of the map, Aaron had instructed them not to reveal the tertiary interactions to us. They carried out his word. In view of this, my response was to make an admittedly limited presentation rather than a complete one. However, a number of people have told me that they would have acted the same way under similar circumstances, as it was clear from the attitude of your colleagues that they were very far from being cooperative. In view of this, we did not feel very kindly disposed towards telling your colleagues the details of our interpretation.

The essential issue, however, concerns the question of the independence of our interpretation. In my lengthy letter of August 9, I assembled all the information I could find with a view towards having you examine this. This included statements from a number of people together with their addresses and telephone numbers. All of these people indicated they were willing to respond to you in writing or in conversation about the authenticity of their

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comments. The reason I sent you such a detailed account was to allow you to check fully and satisfy yourself regarding the independence of our efforts. In particular, Struther Arnott and his group have a fairly full account of the progress which Sung-Hou presented to them two weeks before the meeting. You could satisfy yourself about the progress of the work by writing or talking to him or to his entire group.

As I explained to Sydney in Bombay, one of my reasons for feeling there should be a statement in the public record about the independence of our effort stems from the fact that this was a group effort on our part and I am especially concerned about the reputations of my junior colleagues. If nothing were printed, one could just let the issue slide. But as it stands now, there is a piece in the New Scientist which essentially states that we have plagiarized the data and that statement appears to have the implicit backing of the MRC laboratory. This is the impression given to me by every person who has read the article which now has achieved a widespread distribution in certain scientific circles. We have been unjustly accused of a large number of acts ranging from plagiarizing material at the Madison meeting, plagiarizing material at the Gordon Conference, or to having our work related to a falling out and differences of opinion between Sung-Hou and myself. In addition, Aaron has made public charges of plagiarism in at least four lectures that I know of, and Robertus in one. What happened, however, was that I did not make a full presentation at the Steenbock meeting of the reinterpretation of the map and it is clear that your colleagues likewise did not make a full presentation. The real question is whether the public abuse and irresponsible accusations which we have been subjected to are justified?

I do not feel that we are the only injured parties. As I pointed out to Sydney, this is a "no win" situation on all sides. However, I think that a simple statement from a responsible third party that our work was done independently would effectively terminate the entire affair and I do not think your colleagues would suffer in the process. Alternatively, it would be possible to make a much fuller statement describing in detail all the different events which transpired.

Sydney has undoubtedly spoken to you about many of these things since we had extensive conversations. I would like to hear from you after you have a chance to reflect on this further.

Best wishes,

Yours sincerely,



Alexander Rich

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